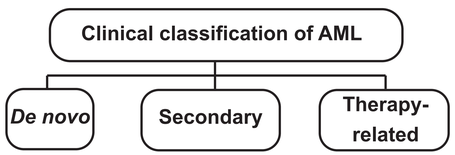
Moleculary-Defined *De Novo* and Secondary Acute Myeloid Leukemia are biologically and clinically different entities

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Introduction

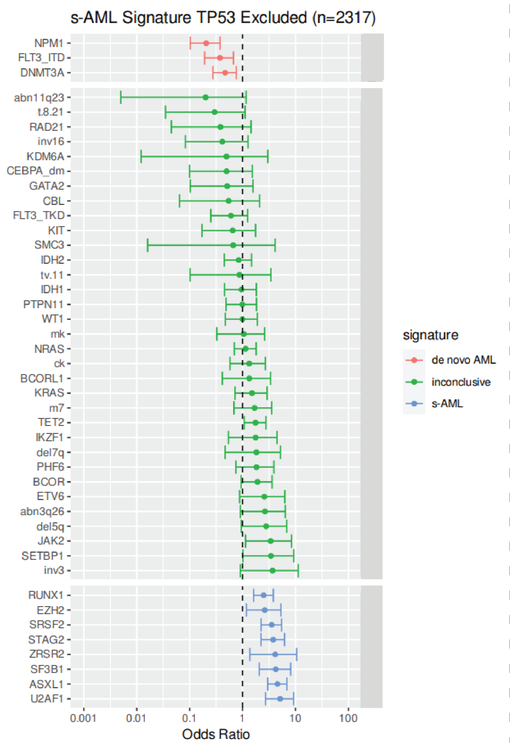


- ☐ sAML evolves from an antecedent hematological disease, whereas *de novo* AML arises in absence of prior disease
- ☐ A broad range of (cyto)genetic abnormalities contributing to AML development have been identified, however, their relation with ontogeny and clinical response has not been studied in larger AML cohorts

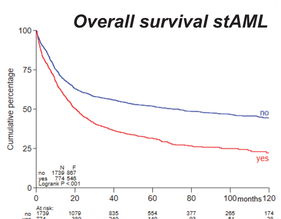
Aim of study

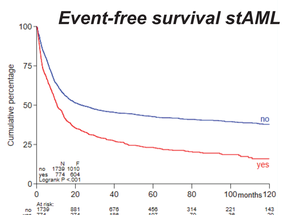
- ☐ Investigate the clinical and biological differences between *de novo* AML and sAML with the underlying hypothesis that (molecularly defined) *de novo* AML and secondary-type AML (stAML) should be considered as two different entities

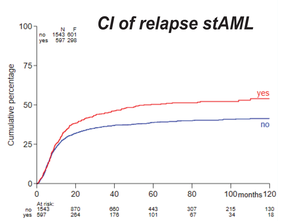
Results



	De novo AML (n=1,705)	stAML (n=742)	p-value
Patient characteristics			
Median Age at diagnosis – yr (range)	52 (15-81)	60 (15-84)	*p*<0.01
Sex – no. (%)			
Male	876 (51.38%)	465 (62.67%)	*p*<0.01
Female	829 (48.62%)	277 (37.33%)	*p*<0.01
Median Number of mutations – no. (range)	2 (0-8)	3 (1-10)	*p*<0.01
Clinical parameters			
Median WBC at diagnosis – × 10^9/L (range)	16.65 (0-340.80)	5.40 (0-510)	*p*<0.01
Median Blasts in bone marrow – (%) (range)	61 (0-100)	42 (0-100)	*p*<0.01
Median Platelets at diagnosis – × 10^9/L (range)	65 (2-1113)	63 (1-998)	*p*=0.298
Median Neutrophils in PB at diagnosis – (%) (range)	18 (0-91)	10 (0-85)	*p*<0.01
Classification			
2017 ELN risk classification at diagnosis – no. (%)			*p*<0.01
Favorable	897 (52.61%)	55 (7.41%)	
Intermediate	574 (33.67%)	130 (17.52%)	
Adverse	211 (12.38%)	547 (73.72%)	
Outcome			
Event Free Survival – no. (%)			*p*<0.01
Complete remission	711 (41.73%)	169 (22.81%)	
Never reached complete remission	194 (11.38%)	164 (22.13%)	
Relapse	589 (33.57%)	291 (39.27%)	
Non-relapse mortality	210 (12.32%)	117 (15.79%)	







Conclusions

- ☐ ***RUNX1, EZH2, SRSF2, STAG2, ZRSR2, SF3B1, ASXL1* and *U2AF1* significantly associated with clinically proven sAML (p <0.01)**
- ☐ **AML carrying these mutations are referred to as stAML**
- ☐ **stAML defines a novel subgroup of AML with a significantly worse clinical outcome**

Methods

- ☐ **2,762 AML patients, who were treated in HOVON or SAKK clinical trials with high intensity chemotherapy, were included**
- ☐ **NGS was performed at diagnosis using the Illumina TruSight Myeloid sequencing panel**
- ☐ **Descriptive statistics were used to describe the clinical characteristics, the Kaplan-Meier method was used for survival analysis**
- ☐ **Multiple forest plots were generated to illustrate the association between individual mutated genes and clinically defined sAML and *de novo* AML**

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